Supplementary Table 1. Implicated Causative Agents in 300 Subjects With Suspected DILI (Regardless of the Causality Scores)

Single prescription agent (n = 217)	Herbal agent(s) (n = 28)	Multiple prescription agents or prescription agent(s) plus herbal agents (n = 55)
Amoxicillin/clavulanate (n = 23)	Right approach	TMP/SMX + levofloxacin
Nitrofurantoin (n = 13)	Green tea (mega tea, Arizona green tea)	Atorvastatin + nitrofurantoin
Isoniazid (n = 13)	Lavender oil, Frankincense oil, Nixia red	Valproate + levofloxacin
TMP/SMX (n = 9)	Melatonex	Moxifloxacin, ciprofloxacin + amoxicillin/clavulanate
Duloxetine (n = 6)	DHEA, M one T (17 α methyl 1-testesterone)	Pregabalin + simvastatin
Valproate (n = 6)	Slim Quick	Metoprolol, diltiazem + alprazolam
Interferon beta (n = 6)	Lipozene	Combivir + nelfinavir (2 cases)
Ciprofloxacin (n = 5)	Airborne, G3 (Gac fruit juice with other Chinese fruit juices)	Isoflurane + lorazepam
Lamotrigine (n = 5)	Dexatrim	Phenytoin + levofloxacin
Methyldopa (n = 5)	Creatine	Levofloxacin + clindamycin
Telithromycin (5)	Formula 2 Multivitamin Complex (Herbalife), Xtra-Cal (Herbalife)	Cyclophosphamide + doxorubicin
Phenytoin (n = 5)	Formula 2 Multivitamin Complex (Herbalife Formula 2), Herbalife Cell Activator, Herbalife shake, Herbalife Total Control, Herbalife Xtra-Cal	Disulfiram + lisinopril
Diclofenac (n = 4)	Methyl masterdrol, VPX Redline Fat Burner	Nitrofurantoin, Source of Life multivitamin mineral + full-spectrum mineral
Terbinafine (n = 4)	Testron-Sx, Proendorphan	Simvastatin + ezetimibe (2 cases)
Levofloxacin (n = 4)	Infinit nutrition formula	TMP/SMX + tetracycline
3 cases each: atomoxetine, azithromycin, oxacillin, atorvastatin, etanercept, mercaptopurine, minocycline, investigational agents	Hydroxycut	Amlodipine + paroxetine
2 cases each: allopurinol, amiodarone, amoxicillin, antithymocyte globulin, doxycycline, nevirapine, ranitidine, celecoxib, desflurane, buproprion, fluoxetine, fluconazole	Niacin	Combivir + Kaletra
1 case each: acitretin, Avalide, itraconazole, amitryptiline, lefluonamide, linezolid, amlodipine, lisinopril, diphenoxylate/atropine, artesunate, bortezomib, meloxicam, methylphenidate, moxifloxacin, cefaclor, cephalexin, cefazolin, cefuroxime, nicotinic acid, oxaprozin, octreotide, ceftriaxone, gentamicin, ketoconazole, pravastatin, promethazine, chlorzoxazone, propafenone, pyrazinamide, cilastatin/imipenam, clindamycin, cyclophosphamide, disulfiram, docetaxel, efavirez, estradiol, fenofibrate, fluvastatin, gabapentin, glipizide, Glucovance, hydralazine, imatinib, interleukin, quinapril, rifampin, salsalate, sertraline, sevoflurane, simvastatin, temozolamide, topiramate, valacyclovir, verapamil, Vytorin, Yasmin	Cimicifuga racemosa	Ciprofloxacin + metronidazole
	Airborne	Cefuroxime + nystatin
	MT-80 (methyl testosterone), Tight yohimbine	Cephalexin + levofloxacin
	Superdrol (methasterone), Anadrol (oxymetholone)	Amoxicillin, Methyl 1-D + Cell-Tech
	Shredded mass	Allopurinol + rosiglitazone
	Oxodrol 2 (2α 17α dimethyl 5α androst 3-one)	Leflunomide + lovastatin
	N.O. Xplode	Leflunomide + Harpagophytum procumberns
	Artemisin, Blue Moon cloves, Kroger-herbal rescue, Blue moon ginger, Black Walnut, Hull tincture, Dandelion root, Cayenne extract, Slippery elm bean	Carbamazepine + fluvoxamine
		Valproate + quetiapine
		Ibuprofen + valdecoxib
		Amlodipine + celecoxib
		Azithromycin + ceftriaxone
		Nitrofurantoin + azithromycin
		Hydroxychloroquine + leflunomide
		Escitalopram + levofloxacin
		Lisinopril, cyclophosphamide + diltiazem
		Testostazine + rosuvastatin
		Amiodarone + atorvastatin
		Creosote + propofol
		Isoniazid + pyrazinamide
		Telithromycin + doxycycline
		Kaletra + Epzicom
		Mercaptopurine + metronidazole
		Sevoflurane + oxcarbazepine
		Telithromycin + nitrofurantoin
		Isoniazid + fenofibrate
	Warm Wood, Cat's claw, Chelex	Telithromycin + amoxicillin/clavulanate
	IP6, All one powder, Pectasol, I-flora, Artemisin, Co Q10 with Hawthrone berry, ImmPower, Digestive enzymes, HCL Cellulase capsules, mannapol, immune enhancing mega, aloe vera formula, flaxseed oil, prostate care, evening primrose oil, Intestinal support, Essiac tea, Flor-Essence	Thiamazole + modafinil
		Gatifloxacin + amoxicillin/clavulanate
		Lansaprazole + modafanil
		Lamotrigine, lovastatin + lithium
		Glibenclamide + doxyclycine
		Azithromycin + TMP/SMX
		Diclofenac, lovastatin + clindamycin
		Valsartan + levofloxacin
		Valacyclovir + Advicor

NOTE. This includes all cases regardless of their level of causality association. It is difficult to describe causality scores in this table; for example, 23 cases of amoxicillin/clavulanate will have different levels of causality scores. See Supplementary Table 2 to see compounds implicated in "unlikely" DILI cases (n = 9).

TMP/SMX, trimethoprim-sulfamethoxazole.

Supplementary Table 2. Characteristics of Enrolled Subjects Who Were Finally Adjudicated as "Unlikely" to Have DILI (n = 9)

	Age	Sex	Biochemical pattern	Peak bilirubin level (*mg/dL*)	Initial implicated agent	Final diagnosis	Comment
1	69	Female	Hepatocellular	0.6	Atorvastatin	Polymyositis	Additional data became available during the follow-up period that suggested an alternate diagnosis.
2	39	Female	Hepatocellular	13.9	Linezolid	Acute hepatitis C	Hepatitis C antibody was negative initially, but both anti-HCV antibody and hepatitis C RNA were positive subsequently and repeatedly. Two years following this episode, she spontaneously cleared her hepatitis C. Patient had a history of recent hospitalization for the treatment of cellulitis and osteomyelitis.
3	51	Male	Mixed	12	Combivir/ Kaletra	Liver failure of unknown etiology	Initially his liver biochemistries improved upon discontinuation of suspected agents. However, he experienced recurrent episodes of jaundice with spontaneous improvement and exacerbation. He eventually died of liver failure at a local hospital.
4	16	Female	Cholestatic	23	TMP/SMX	Recurrent cholestasis	Additional history revealed that this patient had recurrent benign intrahepatic cholestasis with spontaneous exacerbations and had received TMP/SMX on multiple previous occasions.
5	27	Male	Hepatocellular	30	Diphenoxylate/ atropine (Lomotil)	Liver failure of unknown etiology	There was strong suspicion that this individual has consumed but not admitted use of anabolic steroids. Temporal relationship made Lomotil an unlikely culprit.
6	56	Female	Mixed	27	Gentamycin	Acute hepatitis C	Patient's anti-HCV antibody and HCV polymerase chain reaction were positive during the acute episode, but the site investigator considered it to be preexisting chronic infection and acute jaundice was believed to be unrelated to HCV. The Causality Committee adjudicated the acute event as unlikely due to DILI and assigned acute hepatitis C as the more likely diagnosis. Patient had recent hospitalization during which he received gentamicin.
7	62	Male	Hepatocellular	13.3	Isoflurane/ Glipizide	Acute hepatitis C	Anti-HCV antibody tested during the acute event by the referring physician was negative, forming one of the bases for his enrollment, but his enrollment laboratory tests revealed positive anti-HCV antibody and HCV polymerase chain reaction. Patient had recent hospitalization and surgery.
8	51	Male	Hepatocellular	17.1	Levofloxacin	Acute hepatitis C	Anti-HCV antibody testing at enrollment was positive, but the site investigator considered the jaundice episode to be unrelated to hepatitis C because the patient lacked recent risk factors and also the episode had a strong temporal relation to levofloxacin exposure. However, the Causality Committee adjudicated the jaundice episode as unlikely related to DILI and considered acute hepatitis C as the more likely possibility.
9	57	Female	Cholestatic	12.8	Antithymocyte globulin	Unknown	Temporal and exposure to multiple agents and other acute illnesses made DILI an unlikely possibility.

TMP/SMX, trimethoprim-sulfamethoxazole.

Supplementary Table 3. Variables Independently Associated With Severe DILI

Variable	DF	Wald χ^2	Pr > χ^2
Age	1	1.6235	0.2026
Sex	1	0.0011	0.9741
Race	4	1.9542	0.7442
Alcohol	1	6.8321	0.0090
Diabetes mellitus	1	5.0603	0.0245
Duration between exposure and DILI recognition	1	0.4665	0.4946
Pattern of liver injury	2	4.0097	0.1347

Supplementary Table 4. Characteristics of Patients With Suspected DILI Caused by Dietary Supplements as Compared With Single Prescription Agents

	Single prescription agent group (n = 217)	Dietary supplement(s) group (n = 28)	*P*
Age (*y*), mean ± SD	47 ± 19	45 ± 12	.25
Female (%)	61	50	.30
Body mass index (kg/m^2), mean ± SD	26.8 ± 6.7	26.7 ± 5.2	.70
Self-reported race (%)			
White	78	82	.70
Black	10	7	
Asian	5	0	
Preexisting liver disease (%)	5	10	.30
Prior drug allergies (%)	49	46	.80
Diabetes (%)	27	21	.65
Alcohol (%)	49	68	.05
Current smoking (%)	17	11	.56
Days between (median, 25th and 75th percentiles)			
Exposure and DILI recognition	40 (19, 117)	54 (36, 109)	.20
DILI recognition and peak bilirubin level	7 (1, 17)	6.5 (4, 13)	.97
Peak bilirubin level and 50% reduction	17 (8, 33)	19 (11, 58)	.36
Peak bilirubin level and level <2.5 mg/dL	35 (16, 66)	68 (37, 128)	.08
Stevens–Johnson syndrome (%)	1.4	0	1.00
Absolute eosinophil count/μL (mean ± SD)	191 ± 341	128 ± 105	.30
Liver biochemistries, peak values			
ALT (*U/L*), mean ± SD	996 ± 1217	1028 ± 1016	.80
Alkaline phosphatase (*U/L*), mean ± SD	360 ± 305	300 ± 284	.26
Total bilirubin (*mg/dL*), mean ± SD	10.6 ± 9.9	14.7 ± 13.0	.11
INR	1.6 ± 1.5	1.6 ± 2.2	.15
Biochemical pattern (%)			
Hepatocellular	56	63	.80
Cholestatic	24	17	
Mixed	20	21	
Severity of liver injury (%)			
Mild	26	29	.90
Moderate	21	24	
Moderate-hospitalized	31	35	
Severe	16	6	
Fatal	6	6	
Causality assessment (%)			
Definite	34	39	.90
Very likely	37	39	
Probable	14	17	
Possible	10	6	
Unlikely	4	0	
Chronic DILI (%)	12	9	1.00
Death (%)	11	0	.14
Liver transplant (%)	0.6	3.5	1.00